

REMARKS

In response to the Office Action mailed February 26, 2007, Applicant has amended claim 2 solely for the purposes of clarity. Support for all the above amendments may be found throughout the specification as originally filed. No new matter has been added. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the amendments, claims 13, 14 and 26 are withdrawn and claims 1-12, 15-21, 25, and 27-28 are under consideration. Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

Claim Rejections – 35 U.S.C. § 103

Claims 2, 3, 9-12, 15-21, 25, 27 and 28 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Abels *et al.* (WO 97/31582) in view of the abstract of Goetz *et al.* (WO 97/33620), Schultes *et al.* (SPIE, 1994, Vol. 2078, pp.148-157) and further in view of Theodore *et al.* (WO 95/15979). The Action asserts that Abels *et al.* teach the use of ICG for treating vascularized tumors and their metastases, such as Kaposi's sarcoma; adenocarcinoma of the colon, esophagus, breast; neurofibroma and malignant melanoma, comprising administering ICG followed by irradiation with light. Abels *et al.* allegedly teach the light source as recited in claim 3, low fluence rates, and the doses as recited in the instant claims. The Action concedes that Abels *et al.* do not teach conjugation of ICG with targeting antibodies. The Action relies on Schultes *et al.* and the abstract of Goetz *et al.* to overcome this deficiency. Further, the Action asserts that it would have been obvious to the skilled artisan at the time the invention was made to combine the teachings of Theodore *et al.* on pretargeting with the other cited references to arrive at Applicant's invention. As such, the Action alleges that it would have been *prima facie* obvious at the time the invention was made for the skilled artisan to combine the teachings of the cited references to arrive at Applicant's invention.

Claims 1-12, 18-21, 25 and 28 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Abels *et al.* (WO 97/31582) and Schultes *et al.* (SPIE, 1994, Vol. 2078, pp.148-157) in view of Williams *et al.* (US Patent No. 5,576,013), Ruoslahti *et al.* (US Patent No. 6,180,084) and Chen *et al.* (US Patent No. 5,445,608). The Action reiterates the teachings of Abels *et al.* as summarized above and further asserts that Schultes *et al.* teach that administration of the antibody conjugated photosensitizer versus the photosensitizer alone allows for a reduction in the dose of photosensitizer used and the more selective binding to target cells allows for reduced cutaneous phototoxicity. Ruoslahti *et al.* allegedly teach the targeting of cytotoxic agents to angiogenic vasculature of a tumor by means of peptides which bind to the NGR receptor in tumor neovasculature. Williams *et al.* allegedly teach that targeting the blood supply of a lesion is more effective than targeting the lesion itself, and the Action asserts that this is consistent with targeted localization of photosensitizing agents by means of specific ligands which bind to the tumor vasculature. Chen *et al.* allegedly discloses an apparatus comprising a variety of light sources suitable to apply PDT to external surfaces of the body. The Action concludes that it would have been *prima facie* obvious at the time the claimed invention was made to combine the teachings of these references to arrive at Applicant's invention.

Applicant respectfully traverses these rejections on the following grounds.

As an initial matter, Applicant notes that claim 2 has been amended to remove the alternative "or target tissue antigen." This amendment is made without prejudice and solely to expedite prosecution.

The Action fails to establish a *prima facie* case of obviousness (*see In re Mayne*, 104 F.3d 133, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). The Examiner must show (1) that the combined references teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of

prior art references, a teaching, motivation, or suggestion to combine the references must exist (*see In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

At the time of filing the present application, neither cited combination of references would have motivated a person having ordinary skill in the art to arrive at the claimed invention with the requisite reasonable expectation of success. Specifically, Applicant submits that the skilled artisan upon reading Abels *et al.* would conclude that the reference, in fact, teaches away from the present invention. In particular, Abels *et al.* teach specifically the treatment of cancers that present in the skin or just under the skin (*e.g.*, Kaposi's sarcoma, neurofibromas, which usually affect nerves close to the surface of the body, such as nerves of the skin or tissue just below the skin, and melanomas) or adenocarcinomas which are epithelial tumors that are glandular in origin. As such, the cancers appropriate for treatment by the method of Abels *et al.* are not lesions within the vascular system. This is crucial since Abels *et al.* actually teach that light therapy is initiated immediately after administration of the dye so that the dye is still in the area to be treated, *i.e.*, the skin and subcutaneous area (*see* for example, Example 2 at page 26 where irradiation of KS lesions begins 1 minute following the last bolus of dye). Therefore, in fact Abels *et al.* teach away from the present method where "the photosensitizing agent is cleared from the skin and subcutaneous tissues of the subject prior to the irradiation" as presently claimed. Applicant submits that the skilled artisan, upon reading the teachings of Abels *et al.* as a whole, would conclude that their method would not be appropriate for the treatment of vascular lesions as presently claimed in the instant application. As such, Applicant submits that there would be no motivation to combine the teachings of Abels *et al.* with the other cited references.

Neither set of secondary references overcomes the deficiencies of Abels *et al.* Schultes *et al.* merely describe the development of a water-soluble antibody-coupled Phthalocyanine and the use of this compound in *in vitro* and rat model settings of ovarian carcinoma and in breast cancer lesions. Schultes *et al.* fail to cure the deficiencies of Abels *et al.*, in particular by providing no actual teaching with regard to the use of targeting conjugates in methods for destroying target cells in lesions of the vascular system. The abstract of Goetz *et al.* also fails to remedy the deficiencies of Abels *et al.* and in fact provides only a single sentence

describing the use of ICG-antibody conjugates for the treatment of tumors. Similarly, and as noted previously, Theodore *et al.* only generally teaches the use of a pretargeting approach for localizing photosensitizing agents. Thus, none of these references teaches destroying cells that comprise lesions of the vascular system using the claimed methods and targeting agents, particularly in view of the teachings of Abels *et al.*

Concerning Ruoslahti *et al.*, this reference merely describes tumor homing molecules that, in certain embodiments, can be fused to cytotoxic agents. Though numerous agents are listed, only doxorubicin is specifically exemplified and no mention is made of photosensitizing agents as cytotoxic agents nor activation of the photosensitizing agent using irradiation from light sources. There is simply no teaching or suggestion in this reference of using such agents, either targeted or not, for destroying target cells in lesions of the vascular system. Williams *et al.* teach using photosensitizing agents to cut off blood supply to a lesion, essentially by causing blood clots in the vessels that feed a lesion. Applicant submits that the reference teaches that the methods therein are useful for the treatment of tissues containing blood carrying vessels supplying unwanted lesions (*see e.g.*, claim 1). As such, the methods of cutting off blood supply to such a lesion is appropriate. The presently claimed methods are directed to treating unwanted lesions within the vascular system. Therefore, using the methods of Williams *et al.* would have the undesired effect of creating a blood clot within the vascular system. As such, Applicant submits that this reference actually teaches away from the presently claimed methods and in no way remedies the deficiencies of Abels *et al.*

Chen also does not remedy the deficiencies of Abels *et al.* in that it only teaches an apparatus for delivering light-activated therapy. There is simply no teaching in this reference of the presently claimed methods of administering to the subject a therapeutically effective amount of a photosensitizing agent, wherein the photosensitizing agent is conjugated to a ligand that selectively binds to a receptor on target cells of the lesion in the vascular system or administering to the subject a therapeutically effective amount of a first conjugate comprising a first member of a ligand-receptor binding pair conjugated to an antibody or antibody fragment, wherein the antibody or antibody fragment selectively binds to the target cell that comprises the lesion in the arterial vascular system.

Accordingly, Applicant submits that the primary and secondary references, taken individually or for what they teach as a whole, do not teach or suggest the claimed invention and in fact teach away from the present invention. Therefore, Applicant submits that the claimed invention would not have been obvious to the ordinarily skilled artisan at the time of filing. Reconsideration of the claims and withdrawal of the rejections are respectfully requested.

Applicant respectfully submits that all of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,
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